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DEPARTMENT OF ZOOLOGY

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Dear Josh:

Your letter was very welcome. I have thought of you and Esther many times but only recently have I been able to plan something for tomorrow and find that when tomorrow came I had at least a 0.05 chance of getting it done. I can't write about Paris anymore. My spirit plunges when I think of the wonderful freedom we had in that city last year. But if you come east some time a few recollections may be possible in the proper alcoholic atmosphere.

Monod and Cohn felt last year that they had made every effort to keep you in touch with their work. You must be better acquainted with it than I am. At any rate a lot of their thoughts and data have now been put down in a MS for Advances in Enzymology. I admire them both, as persons and as workers. Another American in Paris, Ravin, has been doing well in Ephrussi's lab. He has an interesting story on the regulation of the frequency of exchange between transforming principles.

My own work at the Institute, although really not hampered by the 2400 km. of travelling in our Renault, was no great shakes. I've worked up methods for estimating with some degree of precision the mutation rate of coli from lac^- to lac^+ . But I was unable to find an influence on that rate with substances with and without affinities for lactase and/or a capacity to induce. The gene seems personally pretty inviolate and sensitive only to more general troubles in its environment.

The statistical randomness of this mutation is evident from the fit obtained between the distribution of

numbers of mutants in replicate cultures and that predicted by Lea and Coulson. I find in the literature a few other cases which can be shown to fit and never cease to be astounded by the fact, for the assumptions used in L. and C.'s theory are so simple and unrealistic. The situation is actually quite complex. Armitage (to be published in the J. Roy. Statistical Society) has considered the effect of phenotypic lag and the Oxford statistician, Kendall, has engaged to consider a few additional assumptions. In the meanwhile I am writing up (get to it again tomorrow?) my present thoughts on these matters. By the way, you may be interested to know that, along with the majority of the cases in the literature, the distribution of lac^+ mutants in K12 does not fit L. and C. despite a demonstrable randomness of the mutations. Although K12 lac^- and ML lac^- may be physiologically indistinguishable, I suspect where one is recessive the other is dominant (suppressor) and hope to test this possibility. Tell Esther I'd be happy to hear what she has done with this mutation. Are her results published or could she send me her thesis? I'll send on my MS to her as soon as it is prepared. Her findings re the segregation of lysogenicity allow the most interesting speculations. More power to her.

Back home at Columbia we are carrying forward our selection studies, trying to set up bactogens, chemostats and natural selectors and hope to take another crack at specific induction of mutations. A young fellow, named Wainwright, from Pollack's laboratory, is working with me this year. Pat St. Lawrence is finishing up an analysis of a translocation involving the nucleolar organizer chromosome in Neurospora. It is so complex that I have all I can do to follow her analysis; thank God, the real sponsor is B. McClintock. Sam Gross has begun to work with T_2 and K12 and already has some interesting leads. There are some graduate students in our microbial genetics courses but our group is smaller than of old and we sure miss Kim.

No one here since the days of Dave Perkins has to my knowledge made heterocaryons between 33757 and other biochemical mutants. I believe Dave did; you might ask him. I've searched my own notes and among hundreds of leucineless-independent heterocaryons in a multitude of permutations I find none of the sort you mention. I agree the problem is worth following up. Once a student from Princeton started to do so, but he fell in love and left for medical school after very little progress. Most people do not see this type of problem as interesting. The re-

sult is that my own work stands apart from that of my graduate students and from microbial genetics in general.

Josh, who am I to anticipate the workings of your mind? I can only imagine that you are interested in Streptomyces in order to understand the relation between antibiosis, lysogenicity and recombination. Let me know what you're after when you find something out.

By the way, Tom Nelson writes that he has contacted you about working with you next year. Needless to say I have the greatest confidence in Tom's abilities and am sure you would make a fine combination. If I can be of any help to you in this connection don't hesitate to let me know.

Best regards

Sincerely yours,



Francis J. Ryan

FJR:djj